# Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. N Engl J Med. DOI: 10.1056/NEJMoa2104983

## Appendix

## **Table of Contents**

CDC COVID-19 Response v-safe COVID-19 Pregnancy Registry Team	2
Table S1. V-safe pregnancy registry variables and questions used in the analysis	3
<b>Table S2</b> . Frequency of most common solicited local and systemic reactions	5
<b>Table S3</b> . Frequency of severe solicited local and systemic reactions in v-safe on the day after mRNA COVID-19 vaccination in self-identified pregnant persons and nonpregnant women aged 16–54 years, December 14, 2020–February 28, 2021	7
<b>Table S4</b> . Characteristics of reports to VAERS among pregnant persons following mRNA COVID-19 vaccines, December 14,2020–February 28, 2021	8

### CDC COVID-19 Response v-safe COVID-19 Pregnancy Registry Team

Amena Abbas, M.P.H.<sup>1</sup>, Dayna Alexander, Ph.D.<sup>2</sup>, Katie Arnold, M.D.<sup>3</sup>; Ellen Boundy, Ph.D.<sup>4</sup>; Virginia Bowen, M.D.<sup>5</sup>; Kailyn Brooks, M.P.H.<sup>6</sup>, Cheryl Broussard, Ph.D.<sup>3</sup>; Tara Brown, M.P.H.<sup>7</sup>; Gyan Chandra, M.S.<sup>6</sup>; Dena Cherry-Brown, M.P.H.<sup>3</sup>; Janet D. Cragan, M.D.<sup>3</sup>; Monica DiRienzo, M.A.<sup>8</sup>; Tuyen Do, B.S.<sup>9</sup>; Charise Fox, M.P.H.<sup>3</sup>; Suzanne Gilboa, Ph.D.<sup>3</sup>; Robbie Gray, A.A.<sup>10</sup>; Jennifer Hamborsky, M.P.H.<sup>11</sup>; Anne Hause, Ph.D.<sup>12</sup>; Jennifer Hegle, M.P.H.<sup>13</sup>; Margaret A. Honein, Ph.D.<sup>3</sup>; Obehi Ilenikhena, M.P.H.<sup>14</sup>; Jun Ju, M.S.<sup>15</sup>; Ashley Judge, M.P.H.<sup>3</sup>; Alaya Koneru, M.P.H.<sup>11</sup>; Zanie Leroy, M.D.<sup>16</sup>; Cynthia Moore, M.D.<sup>3</sup>; Anne Moorman, M.P.H.<sup>17</sup>; John Nahabedian, M.S.<sup>3</sup>; Morgan Nail, B.S.<sup>18</sup>; Kimberly Newsome, M.P.H.<sup>8</sup>; Keydra Oladapo, M.P.H.<sup>19</sup>; Nicole Olgun, Ph.D.<sup>20</sup>; Youngjoo Park, M.P.H.<sup>3</sup>; Corinne Marie Parker, Pharm.D.<sup>21</sup>; Emily Petersen, M.D.<sup>6</sup>; Kara Polen, M.P.H.<sup>3</sup>; Jennita Reefhuis, Ph.D.<sup>3</sup>; Penelope Strid, M.P.H.<sup>6</sup>; Ayzsa Tannis, M.P.H.<sup>3</sup>; Letha Thomas, Ph.D.<sup>13</sup>; Lindsey Torre, M.S.P.H.<sup>13</sup>; Emmy Tran, Pharm.D.<sup>3</sup>; Susanna Trost, M.P.H.<sup>6</sup>; Diana Valencia, M.S.<sup>3</sup>; Jennifer Linn Wilkers, M.P.H.<sup>6</sup>; Lauren Zauche, Ph.D.<sup>3</sup>; Sarah Zohdy, Ph.D.<sup>22</sup>

#### **Affiliations:**

<sup>1</sup>Division of Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, CDC; <sup>2</sup>Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; <sup>3</sup>Division of Birth Defects and Infant Disorders, National Center on Birth Defects and Developmental Disabilities, CDC; <sup>4</sup>Division of Nutrition, Physical Activity, and Obesity, National Center for Chronic Disease Prevention and Health Promotion, CDC; <sup>5</sup>Division of Sexually Transmitted Disease Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; <sup>6</sup>Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; <sup>7</sup>Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC; 8Division of Human Development and Disability, National Center on Birth Defects and Developmental Disabilities, CDC; 9Office of the Director, National Center for Emerging and Zoonotic Infectious Diseases, CDC: <sup>10</sup>Office of the Chief Operating Officer, Office of the Director, CDC: <sup>11</sup>Immunization Services Division, National Center for Immunization and Respiratory Diseases, CDC; <sup>12</sup>Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>13</sup>Division of Global HIV and TB, Center for Global Health, CDC; <sup>14</sup>Division of Performance Improvement and Field Services, Center for State, Tribal, Local and Territorial Support, CDC; <sup>15</sup>Division of Field Studies and Engineering, National Institute for Occupational Safety and Health, CDC; <sup>16</sup>Division of Population Health, National Center for Chronic Disease Prevention and Health Promotion, CDC; <sup>17</sup>Division of Viral Hepatitis, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC; <sup>18</sup>Division of Laboratory Sciences, National Center for Environmental Health, CDC; <sup>19</sup> Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention; <sup>20</sup>Health Effects Laboratory Division, National Institute for Occupational Safety and Health, CDC; <sup>21</sup>Division of Preparedness and Emerging Infections, National Center for Emerging and Zoonotic Infectious Diseases, CDC; <sup>22</sup>Division of Parasitic Disease Malaria, Center for Global Health, CDC

Table S1. V-safe pregnancy registry variables and questions used in the analysis.

Variable	Calculated (Y/N)	V-safe pregnancy registry question	Reponses options
1. Age at 1 <sup>st</sup> vaccine	Y	Can you please confirm your date of birth?	
2. Race/Ethnicity	N	What race or races do you consider yourself to be? Select all that apply:	White, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, American Indian or Alaska Native, Unknown, or Decline to respond
	N	Are you Hispanic, Latina, or of Spanish origin? Pick one:	Yes, Hispanic/Latina/Spanish origin, No, Non- Hispanic/not Latina/not Spanish origin, Unknown, or Decline to respond
3. Timing of 1 <sup>st</sup> vaccine dose	Y	Gestational age (based on estimated due date (EDD) if available, then pregnancy end date, then LMP) and date received 1st dose	
4. COVID-19 infection during pregnancy relative to timing of 1 <sup>st</sup> vaccine dose	N	Have you been diagnosed with any of these conditions during your current/recent pregnancy? Please respond by saying yes or no: COVID-19? If Yes: what is the approximate date of diagnosis? If no date, how many weeks pregnant were you when diagnosed? Did you experience any complications during delivery?	
5. Self-reported vaccine priority group	N	Do you fall into any of the groups that were prioritized to receive	Healthcare personnel, A non-healthcare essential worker like a teacher or

		vaccination when it rolled out?	grocery store worker, A medical condition other than pregnancy that increases your risk for severe illness from COVID-19, something else (if other, specify)
6. Pregnancy loss	N	What was the outcome of your recent pregnancy?	Was it a live birth, miscarriage (<20 weeks), stillbirth (≥20 weeks), induced abortion, some other outcome (e.g. ectopic or tubal), declined
7. Congenital anomaly	N	Was a birth defect diagnosed at any time after your baby was born? Can you give me the name(s) or a description of the birth defect?	
8. Preterm	Y	Gestational age (based on EDD if available, then pregnancy end date, then LMP) at birth <37 weeks	
9. Small for gestational age	Y	Gestational age and birth weight (calculated using birthweight below the 10th percentile for gestational age and infant sex using INTERGROWTH-21st Century growth standards)	
10. Neonatal death	N	Is the baby still living? If no, what was the date of death? (<28 days)	

**Table S2**. Frequency of most common solicited local and systemic reactions reported in v-safe on the day after mRNA COVID-19 vaccination by age groups in self-identified pregnant persons and nonpregnant women aged 16–54 years, December 14, 2020–February 28, 2021.

Reaction	Dose 1		Dose 2	
	Pregnant	Nonpregnant	Pregnant	Nonpregnant
	persons	women	persons	women
16–24 years – n (%)	N=391	N=92,194	N=233	N=47,345
Injection site pain	315 (80.6)	77,713 (84.3)	208 (89.3)	41,922 (88.5)
Fatigue	140 (35.8)	36,837 (40.0)	176 (75.5)	35,801 (75.6)
Headache	118 (30.2)	28,785 (31.2)	137 (58.8)	32,725 (69.1)
Myalgia	92 (23.5)	27,871 (30.2)	133 (57.1)	31,945 (67.5)
Chills	35 (9.0)	12,699 (13.8)	88 (37.8)	24,489 (51.7)
Fever or felt feverish	43 (11.0)	13,296 (14.4)	94 (40.3)	25,297 (53.4)
Nausea	49 (12.5)	10,075 (10.9)	81 (34.8)	14,726 (31.1)
Joint pain	32 (8.2)	9,687 (10.5)	67 (28.8)	16,804 (35.5)
Injection site swelling	44 (11.3)	14,286 (15.5)	41 (17.6)	9,880 (20.9)
25–34 years – n (%)	N=10,947	N=272,421	N=8,060	N=172,245
Injection site pain	9,729 (88.9)	235,590 (86.5)	7,409 (91.9)	155,824 (90.5)
Fatigue	3,270 (29.9)	99,834 (36.7)	5,829 (72.3)	131,341 (76.3)
Headache	1,973 (18.0)	74,571 (27.4)	4,555 (56.5)	114,395 (66.4)
Myalgia	1,239 (11.3)	67,552 (24.8)	4,405 (54.7)	117,239 (68.1)
Chills	415 (3.8)	29,549 (10.8)	2,958 (36.7)	88,204 (51.2)
Fever or felt feverish	404 (3.7)	30,430 (11.2)	2,808 (34.8)	87,749 (50.9)
Nausea	726 (6.6)	22,885 (8.4)	2,186 (27.1)	47,459 (27.6)
Joint pain	325 (3.0)	24,757 (9.1)	2,059 (25.5)	65,663 (38.1)
Injection site swelling	659 (6.0)	36,749 (13.5)	928 (11.5)	34,862 (20.2)
35–44 years – n (%)	N=5,288	N=323,015	N=3704	N=209,052
Injection site pain	4,635 (87.7)	272,408 (84.3)	3,416 (92.2)	186,293 (89.1)
Fatigue	1,514 (28.6)	101,279 (31.4)	2,597 (70.1)	150,261 (71.9)
Headache	900 (17.0)	78,344 (24.3)	1,947 (52.6)	127,174 (60.8)
Myalgia	558 (10.6)	64,512 (20.0)	1,950 (52.6)	133,039 (63.6)

Chills	207 (3.9)	28,235 (8.7)	1,339 (36.2)	96,430 (46.1)
Fever or felt feverish	224 (4.2)	28,354 (8.8)	1,230 (33.2)	93,154 (44.6)
Nausea	334 (6.3)	23,027 (7.1)	938 (25.3)	49,561 (23.7)
Joint pain	159 (3.0)	26,186 (8.1)	903 (24.4)	77,283 (37.0)
Injection site swelling	306 (5.8)	40,269 (12.5)	434 (11.7)	42,650 (20.4)
45–54 years – n (%)	N=356	N=321,972	N=276	N=194,989
Injection site pain	283 (79.5)	253,077 (78.6)	241 (87.3)	164,883 (84.6)
Fatigue	98 (27.5)	85,171 (26.5)	170 (61.6)	125,443 (64.3)
Headache	87 (24.4)	71,531 (22.2)	161 (58.3)	108,313 (55.5)
Myalgia	73 (20.5)	55,860 (17.3)	150 (54.3)	109,791 (56.3)
Chills	39 (11.0)	26,149 (8.1)	117 (42.4)	79,522 (40.8)
Fever or felt feverish	38 (10.7)	25,656 (8.0)	110 (39.9)	76,909 (39.4)
Nausea	21 (5.9)	19,265 (6.0)	60 (21.7)	38,210 (19.6)
Joint pain	35 (9.8)	24,962 (7.8)	109 (39.5)	66,102 (33.9)
Injection site swelling	48 (13.5)	39,135 (12.2)	59 (21.4)	39,962 (20.5)

**Table S3**. Frequency of severe solicited local and systemic reactions in v-safe on the day after mRNA COVID-19 vaccination in self-identified pregnant persons and nonpregnant women aged 16–54 years, December 14, 2020–February 28, 2021.

	Dose 1		Dose 2	
	Pregnant persons	Nonpregnant women	<b>Pregnant persons</b>	Nonpregnant women
Reported severe* reaction – n (%)	N=16,982	N=1,009,602	N=12,273	N=623,631
Injection site pain	257 (1.5)	26,049 (2.6)	732 (6.0)	48,934 (7.8)
Fatigue	265 (1.6)	27,461 (2.7)	1,542 (12.6)	91,274 (14.6)
Headache	123 (0.7)	17,817 (1.8)	646 (5.3)	62,512 (10.0)
Myalgia	111 (0.7)	19,579 (1.9)	1,149 (9.4)	85,022 (13.6)
Chills	58 (0.3)	10,737 (1.1)	626 (5.1)	55,412 (8.9)
Measured fever ≥39°C	8 (<0.05)	2,226 (0.2)	67 (0.5)	12,045 (1.9)
Nausea	39 (0.2)	3,757 (0.4)	255 (2.1)	9,872 (1.6)
Joint pain	48 (0.3)	9,512 (0.9)	511 (4.2)	47,118 (7.6)
Injection site swelling	12 (0.1)	1,979 (0.2)	27 (0.2)	4,700 (0.8)
Abdominal pain	16 (0.1)	1,287 (0.1)	38 (0.3)	3,401 (0.5)
Injection site redness	3 (<0.05)	950 (0.1)	16 (0.1)	2,023 (0.3)
Diarrhea	11 (0.1)	1,395 (0.1)	21 (0.2)	1,752 (0.3)
Vomiting	9 (0.1)	776 (0.1)	63 (0.5)	2,086 (0.3)
Injection site itching	4 (<0.05)	375 (<0.05)	6 (<0.05)	709 (0.1)
Rash	1 (<0.05)	210 (<0.05)	0 (0.0)	292 (<0.05)

<sup>\*</sup> Participants were asked to classify the severity of all symptoms except fever as mild (symptoms noticed but weren't a problem), moderate (symptoms limited normal daily activities), or severe (symptoms made normal daily activities difficult or impossible); for this table, fever  $\geq$ 39°C in pregnancy was considered severe.

**Table S4**. Characteristics of reports to VAERS among pregnant persons following mRNA COVID-19 vaccines, December 14,2020–February 28, 2021 (N=221)\*.

Median maternal age in years (range)	33 (16–51)
Trimester of pregnancy at time of vaccination in completed weeks <sup>†</sup>	163
First (0–13 weeks)	81 (49.7)
Second (14–27 weeks)	53 (32.5)
Third (28+ weeks)	29 (17.8)
Vaccine brand (%)	
Pfizer-BioNTech	130 (58.8)
Moderna	90 (40.7)
Most frequently reported nonpregnancy-specific adverse events (%) <sup>‡</sup>	155 (70.1)
Fatigue	44
Headache	43
Chills	30
Pain in extremity	27
Nausea	25
Pain	21
Fever	18
Injection site pain	17
Dizziness	17
Injection site erythema	11
Pregnancy- or neonatal- specific conditions (%)	66 (29.9)
Miscarriage <sup>§</sup>	46
Stillbirth	3
Premature rupture of membranes	3
Vaginal bleeding	3
Fetal hydrops	2
Preterm delivery	2
Neonatal death in 22-week preterm birth	1
Other <sup>¶</sup>	6

<sup>\*</sup>Reports received and processed through February 28, 2021; 1 report with unknown vaccine brand

<sup>&</sup>lt;sup>†</sup> Includes 163 reports where information was available on trimester of pregnancy at the time of vaccination

<sup>&</sup>lt;sup>‡</sup> Not mutually exclusive; more than one adverse event can be assigned to a single report

<sup>§ 37</sup> in first trimester, 2 in second trimester, and 7 where trimester was unknown or not reported

Person was diagnosed with COVID-19 before pregnancy (mild 3-day illness 8 months before delivery) and received dose 2 of Pfizer-BioNTech vaccine one day prior to delivery; onset of

preterm labor symptoms began 2 days before dose 2 and birth occurred 32 hours after dose 2 at 22 weeks and 2 days; reported symptoms following receipt of dose 2 were muscle aches and chills; additional information regarding any adverse events associated with dose 1 of the vaccine were not available

<sup>¶</sup> Other pregnancy- or neonatal-specific conditions include 1 report each of calcified placenta, leakage of amniotic fluid, shortened cervix, gestational diabetes, pre-eclampsia, irregular/painful contractions